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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/003,035	11/01/2001	Danher Wang	22488-712	1240

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/003,035	WANG, DANHER	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-50,52-66 and 79-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-50, 52-66, 79-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/27&09/02/04*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

This is a response to the amendment, paper no. 13, filed 09/27/04. Claims 1-46, 51, , 67-76, 78 and 87-98 have been canceled. Claims 47, 53, 54, 55, 57, 58, 59 and 77 have been amended. Claims 47-50, 52-66, 79-86 are pending before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

New ground rejection:

Claim Rejections - 35 USC § 102

1. Claims 47, 48, 50, 51, 56, 57, and 83 are rejected under 35 U.S.C. 102(a) as being anticipated by Bruce et al. (J. Gene. Virol. 1999, Vol. 80, pp. 2621-2628). on the same ground as stated in the previous rejection.

2. In response to the previous Office Action, applicants amend the claims. A new 102 rejection is issued because the amended claim 57 is also anticipated by the cited prior art.

3. Applicants traverse the previous rejection, and submit that Bruce et al. only teach wild-type HIV antigen. In contrast, the present invention is drawn, inter alia, to recombinant adenovirus comprising mutated HIV envelope protein such as &160, &120 or 41. Bruce et al. do not teach or suggest an adenoviral vector comprising mutated HIV antigen. Hence, Bruce et al. do not teach or suggest each and every aspect of the present invention. Accordingly, Applicant respectfully requests that the rejection should be withdrawn.

4. Applicants' argument has been fully considered; however, it is not found persuasive because the complete HIV envelope protein comprises two domains, one is the cytoplasmic domain and other is the transmemebrane domain. The envelope protein disclosed by Bruce et al. only contains the cytoplasmic domain, which is different from the complete HIV envelope protein since it lacks the transmembrane domain. Therefore, it is considered as a mutated HIV envelope protein.

5. Regarding to claim 57, because, the envelope protein gp120 disclosed by Bruce inherently comprises several loops, which meets the limitation of claim 57. Therefore, the prior art anticipates claims 47, 48, 50, 51, 56, 57, and 83.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 47, 48, 50, 56, 57, 60, 62, 79-86 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Bruce et al. (J. Gene. Virol. 1999, Vol. 80, pages 2621-2628), LaRosa et al. (Science 1990, Vol. 249, pp. 932-935), Ivanoff et al. (US Patent No. 5,141,867A), Gorzigia et al. (J. Virol. 1999, Vol. 73, No. 7, pp. 6048-6055) and Ramshaw et al. (US Patent No. 5,866,131A).

8. Claimed invention is directed to a recombinant bicistronic adenovirus vector made by a replication-incompetent adenovirus comprising two HIV sequences, wherein a first HIV sequence encoding a first HIV antigen, which is expressed under a first promoter; and a second HIV sequence encoding a second HIV antigen, which is under a second promoter control. The HIV antigen can be same or different. The adenovirus further comprises an immunostimulatory sequence.

9. Bruce et al. disclose a recombinant bicistronic adenovirus vector made by a replication-deficient adenovirus in which the Rev-responsive element and the envelope glycoprotein gp120 of HIV-1 IIIB strain ranging from nucleotide 5736-8473 were inserted in tandem into the deleted E3 region through splice-donor site and under two powerful cytomegalovirus (CMV) immediate early (IE) promoters respectively. HIV envelope protein and rev proteins are different HIV antigenic proteins, and the Rev protein is also a HIV regulatory protein. Each of them is regulated under a separate CMV promoter (See sections of Methods and Results on pages 2622-2625. Especially see lines 4 to 37 on 1st col. of page 2622 and lines 12 on 1st col. of page 2625

through line 28 on the 1st col. of page 2626 and Fig. 4 on page 2625). Bruce et al. further teach that the rev provided by bicistronically result in a good expression of HIV envelope protein in vitro and a humoral immune response was detected after two immunizations with the bicistronic recombinant adenovirus vector comprising both envelope and rev proteins (RA142) (See abstract, Figs. 2-4 on pages 2624-2625).

10. Gorzigia et al. disclose that a recombinant adenovirus vector can be constructed with E1, E2a, E3 and all of E4 except open reading frame 3 (See Abstract and Fig. 1 on page 6049), and an insertion of any foreign gene into any of this deleted region can be expressed (See section of RESULTS on pages 6050-6052). They suggest that the additional deletion of E4 on the E1 and E2a deletion background may be beneficial in decreasing immunogenic and improving safety and toxicity profiles, as well as increasing transgene capacity in gene therapy.

11. LaRosa et al. teach a V3 loop of HIV comprising an antigenic fragment with a 100% homology to the SEQ ID NO: 25 as claimed in the current application.

12. Ivanoff et al. (US Patent No. 5,141,867A) teach a transmembrane domain of HIV envelope protein gp41, which has 100% homology to the SEQ ID NO: 75. They also teach this transmembrane domain of HIV gp41 can be used as an antigen to raise a monoclonal antibody (Claims 1-3 and example 2 on col. 7).

13. Murphy et al. disclose a signal peptide (SEQ ID NO: 6) having 100% homology to the claimed signal peptide of SEQ ID NO: 74. They also teach that the use of a heterologous signal peptide fused to a recombinant protein can increase the recombinant protein expression, such as the expression of the recombinant HIV envelope protein gp120 fused with the heterologous signal peptide increase 20-30 folds (See lines 12-42 on col. 15 and lines 18-46 on col. 13).

14. Ramshaw et al. disclose a method for stimulating the immune response of a host by using a preparation of a vaccine vector including adenovirus vector that comprises a first heterologous gene sequence encoding an antigen polypeptide, including HIV-1 antigen polypeptide, and a second heterologous sequence encoding a cytokine selected from a group consisting of IL-1, IL-2, IL-4, IL-5, INF-λ etc. (See claims 1-4, 7, 10-12, 14-17 and lines 62-67 in col. 5).

1. Therefore, in order to produce an enhanced immune response by using a replication-incompetent bicistonic adenovirus vector, it would have been obvious for an ordinary skill person in the art to be motivated to combine all already established knowledge taught by the

cited prior art above to construct a replication-incompetent adenovirus vector with E1 and E4 mutations and express two antigenic sequences with one cytokine sequence with no unexpected result. Because art already established that an adenovirus vector can be made by E1 and/or E4 deletion. Especially, the prior art teaches that the protein expression can be same and with less toxicity if more adenovirus endogenous structural proteins can be deleted because the more endogenous protein is deleted, the less toxicity and vector-induce host immune response can be obtained as reported by Gorigilia et al (See Abstract). All of the claimed sequences are also already known and well described as an antigenic or functional peptide or polypeptide.

2. Hence, the claimed invention as a whole is prime facie obviousness without unexpected result.

Conclusion

3. The claims that are free of rejection, are not in condition for allowance because they depend on the rejection claims. No claims are allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao Qun Li
12/11/2004

James C. Housel
JAMES HOUSEL 12/13/04
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Petition under (37 C.F.R. §1.48(a))

Petition under (37 C.F.R. j1.48(a)) for request to correct the inventorship filed on May 24, 2004 has been reviewed. Since it is properly filed with a new oath/declaration singed by all the inventors and assignee. The fee for the petition is paid timely. The petition is granted by the supervisory examiner of art Unit 1846, James Housel.

James Housel
SPE of Art Unit 1648
December 12, 2004